Reviewer's report

Title: Primary small cell carcinoma of esophagus: clinicopathological study of 44 cases

Version: 2
Date: 1 November 2013
Reviewer: Rupert Langer

Reviewer's report:

Major compulsory revisions:
- Definition of SCCE: according to the WHO classification, SCCE is regarded as neuroendocrine carcinoma. The authors describe positivity for neuroendocrine markers, but in its current form, one cannot see if this does not account for every tumor. Was every tumor with small cell morphology confirmed by neuroendocrine markers?
- English language needs major corrections throughout the text. Overall, the paper would benefit from a proper editing. In its current form it appears to be sloppily written.
- The rationale for the link between SCCE and Lgr5 is not clearly described and seems to be very arbitrary. Please address to that issue in the discussion (Any data about LGR5 in other types of esophageal cancer on the one hand and small cell/neuroendocrine cancer on the other hand?)
- Moreover, the authors should consider evaluating gene expression of Lgr5 with additional RT-PCR. Do the authors have information about other stem cell markers such as CD 133?
- How many cases with esophageal cancers have been treated during this time period? It would be interesting to know the percentage of SCCE compared to "conventional" esophageal cancer (squamous/adenoc). It is recognized that the presented collection is very large. The paper would benefit from a better description of the collective (also in comparison to a) other esophageal cancers and b) other small cell carcinomas.
- The conclusion is not clear.

Minor essential revisions:
- How was the cut off for IHC set? arbitrarily? How was the distribution of the staining scores?
- The authors conclude that high Lrg5 levels are associated with chemotherapy response. It would be more convenient for the reader to have this information also in the results section and not only in the discussion part.
- Figure 2: Pictures are nice giving small cell morphology. Negative and positive staining would be sufficient. The current description is misleading suggesting that all patients with for example stage I tumors have negative staining and all
patients of stage IV tumors have positive staining.

discretionary revisions:
- none

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.